

**REMARKS**

**A. Regarding the Amendments**

Claims 1, 3-5, 8, 10, 11 and 16-20 have been amended as set forth in the attached "Version With Markings To Show Changes Made." As amended, the claims are supported by the specification and the original claims. Applicants submit that the amendments to the claims are for clarity and should not be construed as amendments affecting patentability under Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) (en banc). Thus, upon entry of the amendments, claims 1-8, 10-13 and 15-20 will be pending.

**B. Rejection Under 35 U.S.C. § 112**

Applicants respectfully traverse the rejection of claims 1-8, 10-13 and 15-20 under 35 U.S.C. § 112, first paragraph, for containing subject matter allegedly not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time of filing of the Application. In particular, it is alleged in Paper No. 14 that claims 1, 5 and 10 contain reference to "fumaric acid dry crystals, moisture containing fumaric acid or fumaric acid aqueous suspension," as allegedly not supported in the specification. Applicants respectfully disagree.

The Examiner's attention is respectfully drawn to page 14 of the application, lines 22-24. The paragraph states, "The fumaric acid to be added may take any of the following forms: dry crystals, moisture-containing crystals, aqueous suspension or the like." Therefore, amendment of the language "adding fumaric acid to said solution" to "adding fumaric acid dry crystals, moisture-containing fumaric acid crystals, or a fumaric acid aqueous suspension" is supported by the types of fumaric acid specified in the specification. Claim 5 is dependent from claim 1 and only clarifies the cooling specified in the claim. Claim 10 is another independent claim which previously read "adding fumaric acid." Accordingly, the language specifying the form of

fumaric acid is supported by the language of the specification on page 14, as set forth above with regard to claim 1. Therefore, claims 1, 5 and 10 meet the written description requirement of 35 U.S.C. §112, first paragraph. Accordingly, removal of the rejection is requested.

Additionally, claim 18 is rejected under 35 U.S.C. §112, first paragraph, as containing "infinite recycling" that is allegedly not contained in the specification. Applicants respectfully disagree. The Examiner's attention is respectfully drawn to the specification at page 23, lines 10-17. This paragraph discusses the recycling of the mother liquor "10 times or more." There is no limitation as to the number of times this recycling can be performed. Therefore, the language of claim 18 is supported by the specification and claim 18 meets the written description requirement of 35 U.S.C. §112, first paragraph. However, in the interest of advancing prosecution, claim 18 has been amended. Accordingly, removal of the rejection is requested.

Applicants respectfully traverse the rejection of claims 1-8, 10-13 and 15-20 under 35 U.S.C. § 112, first paragraph, for allegedly being non-enabled. As set forth above, the claims are supported by the specification, such that one of skill in the art would have been able to practice the invention at the time of filing of the application. Accordingly, removal of the rejection is respectfully requested.

Applicants respectfully traverse the rejection of claims 1-8, 10-13 and 15-20 under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to point out and distinctly claim the subject matter of the invention.

Specifically, claims 1 and 10 are allegedly vague, indefinite and confusing in the recitation of the term "a temperature of said solution reaches a range of between 50 to 130°C." The Examiner's attention is respectfully drawn to the amended language of claim 1. As amended, lines 4-5 of claim 1 contain the phrase, "to a temperature within the range of 50 to 130°C." As amended, it is submitted that it is clear that the ammonium L-aspartate solution is brought to a temperature within the range of 50-130°C. From lines 10-11 it is clear that the

temperature of the solution is maintained within this range. Similar amendments have been made to claim 10. Accordingly, it is respectfully submitted that these claims are clear. Withdrawal of the rejection is therefore respectfully requested.

Additionally, claims 1 and 10 are rejected for recitation of the phrase "cooling or permitting cooling," as it is alleged that the term is redundant. It is respectfully submitted that the term is not redundant, as can be seen in the specification, for example, at page 17, lines 9-18, and in the examples. In claim 1, since a shearing force is applied to the mixture, L-aspartic acid crystals can be obtained by allowing the mixture to stand and/or cooling the homogenous solution. In this case, the cooling rate is not particularly limited, though the specified rate disclosed in claim 5 is preferred. In claim 10, however, a shearing force is not applied to the mixture, and the mixture must be cooled at a specific rate to be obtain high quality L-aspartic acid crystals. Therefore, the phrase has been amended to "allowing to stand and/or cooling" in claim 1 and to "cooling" in claim 10. Accordingly, withdrawal of the rejection is respectfully requested.

Claim 1 has been rejected as allegedly confusing in the antecedent basis for fumarate at line 8. The Examiner's attention is respectfully drawn to the amendment to claim 1, where the language now clarifies that the fumarate is the total molar amount of ammonium fumarate. This amendment is supported, for example, at page 13, lines 19 to 25. As set forth in the specification, the ammonium fumarate solution is subjected to an enzymatic reaction using aspartase to convert the solution into the ammonium L-aspartate solution. However, since a conversion ratio of around 90% will be sufficient for the crystallization of L-aspartic acid, even if not reaching the equilibrium, a small amount of ammonium fumarate remains in the ammonium L-aspartate solution, which is easily recognized by one of skill in the art. To this solution containing the ammonium L-aspartate and a little amount of ammonium fumarate, fumaric acid is added in a molar ration to those amounts. As amended, it is respectfully submitted that the

language of the claim contains a proper antecedent basis and withdrawal of the rejection is respectfully requested.

Claims 5 and 10 are rejected as allegedly lacking a certain antecedent basis for the term "thereto." The Examiner's attention is respectfully drawn to amended claims 5 and 10, wherein this term is a part of the text that has been removed from those claims. Accordingly the rejection is submitted as moot and removal is respectfully requested.

Claim 5 is rejected as lacking a basis in claim 1 for "a cooling step." Applicants respectfully draw the Examiner's attention to the amended claims, where claim 5 has been amended to read "wherein said cooling." Accordingly, claim 5 has antecedent basis in claim 1. Additionally, it has been asserted that it cannot readily be ascertained how the temperature rate is to be calculated or assessed. Applicants respectfully submit that the rate in the claim is 0.1 to 5°C per minute and that one of skill in the art will know how to effect cooling at this rate and to measure the same. As the rate is simply a number of degrees per minute, the rate of a particular cooling could be determined by measuring the drop in temperature over a given period of time. Accordingly, it is respectfully requested that this rejection be withdrawn.

Claim 10 is also rejected as allegedly vague and indefinite in use of the term "to crystallize L-aspartic acid for crystallizing L-aspartic acid." It is respectfully submitted that this rejection is moot, as the term is no longer contained in the claim. Removal of the rejection is therefore respectfully requested.

Claim 17 is rejected as allegedly confusing in use of the term "a substrate solution." It is respectfully submitted that this term no longer appears in the claim and therefore the rejection is moot. Removal is respectfully requested. Claims 17 and 18 are rejected as allegedly uncertain for use of the term "a mother liquor" in those claims. The examiner's attention is respectfully drawn to the amended claims, where the term now reads "the mother liquor." Accordingly, the claims are clear and withdrawal of the rejection is respectfully requested.

Claim 19 is rejected as allegedly unclear for use of the terms "a washing liquid" and "recycling." As amended, these terms are no longer contained in the claim and the amended language clearly sets forth the subject matter of the claim. Therefore withdrawal of the rejection is respectfully requested.

Claims 1 and 10 are rejected as allegedly containing an unclear molar ratio. Applicants respectfully disagree. It is respectfully submitted that, although the claim language was clear previously, as amended it is even clearer. Claims 1 and 10 now read that fumaric acid is added to the heated solution in a molar ratio of 0.4 - 0.8 to the total molar amount of ammonium L-aspartate and ammonium fumarate in the solution. It would be clear to one of skill in the art that the total molar amount of ammonium L-aspartate and ammonium fumarate in the solution must be known, then fumaric acid is added in a ratio of 0.4 - 0.8 moles to every 1 mole of ammonium L-aspartate and ammonium fumarate in the solution. One of skill in the art would know how to calculate such a molar ratio and add the appropriate amount of fumaric acid. Accordingly, withdrawal of the rejection is respectfully requested.

Additionally, claims 1 and 10 are rejected as confusing with regard to the terms "moisture containing" and "aqueous suspension." Applicants respectfully disagree. It is stated in Paper No. 14 that the distinction between these two terms is not clear, even when reading the claims in light of the specification. The Examiner's attention is respectfully drawn to the paragraph beginning on page 14 and continuing to the bottom of page 15. In that paragraph the various moisture contents of dry crystals, moisture containing crystals and aqueous suspensions are discussed. In particular, it is stated that the moisture content of the moisture-containing crystals is preferably 3% by weight or more, not to exceed 40% by weight. Additional preferred ranges within these extremes are given on page 15. In contrast, the moisture content of the aqueous suspension is preferably 50% or more by weight, preferably not to exceed 200% by weight. Accordingly, it would be clear to one of skill in the art that the difference between moisture-containing crystals and aqueous suspension would be the moisture content. Therefore, it is

respectfully submitted that use of these two terms is clear and withdrawal of the rejection is respectfully requested.

Claim 8 is rejected as allegedly unclear for the manner and use of the term "the crystallization step." It is respectfully submitted that, as amended, the claim no longer contains this term. Accordingly, the rejection is submitted as moot and withdrawal is respectfully requested.

Claim 1 is also rejected as lacking a proper antecedent basis for the term "said solution between..." It is respectfully submitted that this term is not found in the previously pending or amended claim. It is believed that the term the Examiner was referring to is no longer present in the claim, as amended, and therefore the rejection is submitted as moot and removal of the rejection is respectfully requested. However, if the language the Examiner is referring to is still present in the claim, clarification of the rejection is requested.

In light of the above arguments, it is respectfully submitted that claims 1-8, 10-13 and 15-20 meet the definiteness requirement of 35 U.S.C. §112, second paragraph. Accordingly, withdrawal of the above rejections are requested.

**C. Rejection Under 35 U.S.C. § 103**

Applicants respectfully traverse the rejection of claims 1-8 and 10-13 under 35 U.S.C. 103(a) as allegedly unpatentable over Nore et al., in light of Brun et al., Pavia et al., and Tan et al. In order for an invention to be obvious, the differences between the subject matter of the application and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the art. In order to meet this standard, the combination of references must teach or suggest all of the elements of the claimed invention. It is respectfully submitted that Nore et al., in light of Brun et al., Pavia et al., and Tan et al. do not teach or suggest all of the elements of the claimed invention.

It is alleged in Paper No. 14 that Nore teaches a method of producing aspartic acid wherein fumaric acid is added to ammonium aspartate followed by heating and crystallization. However it is respectfully submitted that Nore, neither alone, nor in combination with the Brun et al., Pavia et al., and/or Tan et al references teaches or suggests all of the elements of the claimed invention.

In general, fumaric acid has a markedly lower solubility in an aqueous mixture and at room temperature (see, for example, col. 1, lines 52-55 of Brun et al.). Nore et al., therefore used alcoholic fumaric acid (at 45°C in the example), in which fumaric acid was dissolved in an alcoholic solvent, and was added to ammonium aspartate (at 20-80°C) to increase the solubility of fumaric acid in an aqueous mixture.

On the other hand, in the present invention, fumaric acid in the form of dry crystals, moisture-containing crystals or an aqueous suspension is added to a heated ammonium L-aspartate solution (50 to 130°C) without using an alcoholic solvent. Nore, et al., in combination with the Brun et al., Pavia et al., and Tan et al references, does not teach or suggest a heated ammonium L-aspartate solution or lack of an alcoholic solvent.

As no alcoholic solvent is used, the present invention has many advantages. With use of an alcoholic solvent, the solvent may cause the degeneration of the enzyme aspartase. In contrast, in the claimed invention, the aspartase is not inhibited nor deactivated by any alcoholic solvent. Additionally, when an alcoholic solvent is used, the alcoholic component must be separated from the mixture for the enzymatic reaction with aspartase. The separation of the alcoholic component is difficult, so the mixture is required at a high-purity. However, in the present invention, the separation step of an alcoholic component is not required. Therefore, the method of the present invention is simple and can be performed at a very low cost.

In addition, it is also alleged that Nore et al. indicate that the temperature drops 20°C in 15 minutes during precipitation. However, in the example in Nore, it is documented that "after

stirring for 15 minutes, the mixture is cooled to 30°C.” The description means that stirring is carried out for 15 minutes, and the mixture is subsequently cooled to 30°C for unspecified time. “Fifteen minutes” is not cooling time, but stirring time before cooling. Although the stirring may cool the solution, a cooling step is taught after the stirring step. To be more specific, it is indicated by the following formula.

$$\text{total time} = \text{stirring time (15 min)} + \text{cooling time (X min)}$$

The above total time is unclear because the time for cooling to 30°C is not described in Nore et al. Thus, it is impossible to determine the cooling rate in Nore et al. Accordingly, Nore et al. does not teach or discuss the cooling rate of the claimed invention.

Additionally, the Examiner's attention is drawn to Nore et al., where a prior crystallization of the L-aspartic is not required before filtration. In Nore et al. the L-aspartic acid formed precipitates and crystallizes instantaneously (col. 1, lines 18-22 and lines 49-52). Therefore, Nore et al. teach that the precipitates and crystals of L-aspartic acid are obtained without steps of crystallizing. Thus, the cooling is performed to filtration under vacuum in example 1 and is not required for crystallization.

In contrast, in the claimed invention, the homogeneous solution, which is obtained by applying a shearing force to the solution for a short time, causes a salt exchange reaction between L-aspartic acid and fumaric acid. Subsequently, the solution is supersaturated by allowing to stand and/or cooling the solution, and L-aspartic acid crystals are precipitated.

Nore et al. does not teach or suggest all of the elements of the claimed invention. Specifically, Nore et al. does not teach a use of a solvent other than an alcoholic solvent, does not teach addition of fumaric acid to a heated ammonium L-aspartate solution, does not teach the cooling rate of the claimed invention and does not teach crystallization before filtration. It is also submitted that Nore et al., taken in combination with the Brun et al., Pavia et al., and/or Tan et al



references, still does not teach or suggest all of the elements of the claimed invention and that the claimed invention is therefore not obvious in light of these references.

Specifically, the Examiner alleges that Brun et al. teach a similar process using a temperature of 135°C and gradual cooling of the reaction productions (e.g., examples). However, there is only the following description in the example: "The temperature was maintained at 135°C for 10 minutes. The reactor was then permitted to cool and discharge was carried out when the temperature of the reaction mixture reached 88°C". Thus, "10 minutes" is the time for maintaining the reaction mixture at 135°C, and not the time for cooling the reaction mixture from 135°C to 88°C. Accordingly, there is no disclosure or suggestion in Brun et al. regarding gradual cooling within specified time.

In addition, Brun et al. teach that the mixture was stirred using a magnetic stirrer. Since fumaric acid is added to a non-heated ammonium L-aspartate solution, it is necessary to stir the mixture for a long time, in order to obtain a homogenous solution (for example, stirring time is 1 h at 20°C, and stirring time is 1.5 h at 100°C, Table 1). In contrast, in the claimed invention, an ammonium L-aspartate solution is heated prior to addition of fumaric acid and maintained at a temperature of between 50-130°C. Fumaric acid is then added to the heated ammonium L-aspartate solution and a shearing force is applied to the mixture. As a result, fumaric acid is dissolved in the ammonium L-aspartate solution extremely evenly and rapidly. For example, the time required for mixing and dissolution is approximately 0.1 to several seconds only using a line mixer, whereas the time is approximately 1 to 10 minutes only using an agitation vessel (page 16, lines 12-15).

Additionally, the Examiner has cited Pavia et al. as teaching that it is routine in the art of crystallization to remove the solvent in a crystallization process by a variety of methods, including reduced pressure and the Examiner has cited Tan et al. as teaching the use of condensing and recycling to maximize the yield of crystallized product. However, as set forth above, Nore et al.,

in light of Brun et al., Pavia et al., and Tan et al. do not teach or suggest all of the elements of the claimed invention.

The claimed invention teaches a method of preparing aspartic acid wherein fumaric acid is dissolved in the heated ammonium L-aspartate solution and L-aspartate is crystallized under specific condition without an alcoholic solvent, which was not taught or suggested by the cited prior art. Additionally, the method of the present invention can successfully produce a needle-like L-aspartic acid crystal having mainly 30-1000  $\mu\text{m}$  (See, line 18-19 in page 10). Therefore, in filtration of needle-like L-aspartic crystals of this size, liquid passes through them quickly. Thus, their purity can be improved by simple washing operations. This effect cannot be obtained in any of the cited references, nor was it taught or suggested by the cited references. Accordingly, the claimed invention is not obvious in light of in light of Brun et al., Pavia et al., and Tan et al.

In re Application of :  
Mukouyama et al.  
Application No.: 09/408,142  
Filed: September 29, 1999  
Page 14

PATENT  
Attorney Docket No.: HIRA1140

**CONCLUSION**

In summary, for the reasons set forth herein, Applicants maintain that claims 1-8, 10-13 and 15-20 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. A method for producing L-aspartic acid comprising:  
treating an ammonium fumarate solution with aspartase to generate an ammonium L-aspartate solution;  
heating said ammonium L-aspartate solution to [until] a temperature within the range of [said solution reaches a range of between] 50 to 130°C;  
adding fumaric acid in the form of dry crystals, moisture-containing [fumaric acid] crystals, or an [fumaric acid] aqueous suspension to said heated ammonium L-aspartate solution in a molar ratio of 0.4 to 0.8 to the total molar amount of ammonium L-aspartate and ammonium fumarate [fumarate and the L-aspartate] contained [therein] in the ammonium L-aspartate solution to form a resultant mixture and applying a shearing force to the resultant mixture [to obtain a homogenous solution], while maintaining the temperature [of said solution] between 50°C and 130°C to obtain a homogenous solution;  
allowing to stand and/or cooling [or permitting cooling of] said homogenous solution to crystallize L-aspartic acid, thereby obtaining a suspension containing L-aspartic acid; and separating L-aspartic acid crystals from said suspension.
3. The method according to claim 1, wherein said homogenous solution is further maintained at 50 to 130°C for 0.1 second to 1 hour.
4. The method according to claim 1, wherein [fumaric acid crystals] said fumaric acid and said heated ammonium L-aspartate solution are mixed continuously.
5. The method according to claim 1, wherein said cooling [step] is performed at a rate of 0.1 - 5°C/min until the temperature of said homogenous solution is brought to between 25 and 100°C [from the temperature at which fumaric acid dry crystals, moisture-containing fumaric

acid crystals, or fumaric acid aqueous suspension is added thereto to the temperature at which crystallized L-aspartic acid is separated therefrom, to thereby crystallize L-aspartic acid].

8. The method according to claim 1, wherein the [crystallizing step is] allowing to stand and/or cooling and separating are performed by a continuous method.
10. A method for producing L-aspartic acid comprising:
  - treating an ammonium fumarate solution with aspartase to generate an ammonium L-aspartate solution;
  - heating said ammonium L-aspartate solution to [until] a temperature within the range of [said solution reaches a range of between] 50 to 130°C;
  - adding fumaric acid in the form of dry crystals, moisture-containing [fumaric acid] crystals, or an [fumaric acid] aqueous suspension to said ammonium L-aspartate solution; and
  - cooling [or permitting cooling of] said resultant mixture at a rate of 0.1 to 5 °C/min to between 25 and 100°C [from the temperature at which fumaric acid dry crystals, moisture-containing fumaric acid crystals, or fumaric acid aqueous suspension is added thereto to crystallize L-aspartic acid for crystallizing L-aspartic acid], thereby obtaining a suspension [containing] containing L-aspartic acid; and
  - separating L-aspartic acid crystals from said suspension.
11. The method according to claim 10, wherein said resultant mixture [the solution from which L-aspartic acid is deposited] is a homogenous solution.
16. The method according to claim 1, further comprising washing the L-aspartic acid crystals obtained in said separating [step] with water.

17. The method according to claim 15, wherein [a] the mother liquor obtained by said filtration is [recycled] used as a source of ammonium fumarate [substrate solution for L-aspartic acid production].
18. The method according to claim 17, wherein [the recycling of a] the mother liquor [obtained by said filtration] is used repeatedly [repeated 2 times, or more].
19. The method according to claim 16, [further comprising recycling of a] wherein the washing liquid obtained after washing [by said washing step] is used as a source of ammonium fumarate.
20. The method according to claim 8, wherein said continuous method is performed by feeding said homogenous solution [in] into a suspension containing L-aspartic acid [and evaporating said suspension to remove water under reduced pressure].